

Radiation Segmentectomy for Early-Stage Hepatocellular Carcinoma in Patients with Non-Alcoholic Steatohepatitis versus Chronic Viral Hepatitis

Cynthia De la Garza-Ramos, MD¹; S. Ali Montazeri, MD MPH¹; Kaitlyn R. Musto, PA-C¹; Melissa D. Kapp, APRN¹; Andrew R. Lewis, MD¹; Gregory Frey, MD MPH¹; Ricardo Paz-Fumagalli, MD¹; Sumera I. Ilyas, MBBS²; Beau B. Toskich, MD¹

¹Division of Interventional Radiology, Mayo Clinic Florida, FL, USA; ²Division of Gastroenterology and Hepatology, Mayo Clinic Rochester, MN, USA

BACKGROUND

HEPATOCELLULAR CARCINOMA (HCC)

- Global impact¹:
 - 7th highest incidence
 - 4th highest cancer-related mortality
- Most common risk factor: **chronic liver disease**
 - Viral hepatitis
 - NASH
- Optimal management:
 - Multidisciplinary &
 - Personalized
- Variables to consider during treatment decision-making include:
 - Tumor size and location
 - Extent of HCC spread
 - Patient functional status
 - Degree of liver disease
 - Treatment intent

And an emerging variable...

ETIOLOGY OF LIVER DISEASE

- Studies suggest differences in outcomes between populations with non-viral versus viral-related HCC treated with systemic or immunotherapies^{2,3,4}
- NASH-related HCC:
 - Altered T-cell responses
 - Impaired immune surveillance²
- Real-world data analysis by etiology of liver disease comparing HCC outcomes with atezolizumab/bevacizumab vs lenvatinib⁴:
 - Longer time-to-progression (TTP) and overall survival (OS) in viral-related HCC with atezolizumab/bevacizumab
 - Longer OS in NASH-related HCC with lenvatinib

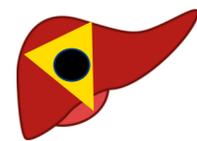
RADIATION SEGMENTECTOMY

- Ablative radioembolization to two Couinaud hepatic segments or less; minimal/no exposure to surrounding untreated parenchyma
- Y90-containing glass microspheres: FDA approved for solitary HCC in patients with preserved liver function
- Recent inclusion in BCLC and NCCN guidelines
- Early-stage HCC: efficacy comparable to other ablative modalities and surgical resection
- Complete pathologic necrosis (CPN) associated with doses >500 Gy and specific activity (up to 8-day decay)⁵
- Prospective evidence shows superior tumor control and survival with radioembolization compared to chemoembolization for BCLC A & B disease⁶

PURPOSE

Knowledge gap: *Does the natural progression of metabolic-related versus viral-related liver disease play a role in HCC response to ablative radioembolization?*

OBJECTIVE



Investigate if the outcomes of radiation segmentectomy for treatment-naïve, early-stage differ in patients with NASH- vs HCV-related liver disease.

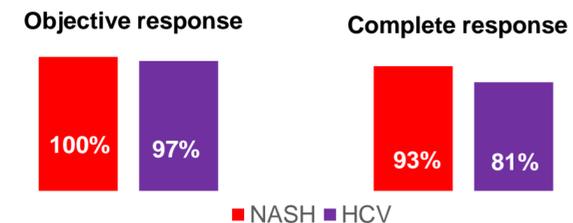
METHODS

- This is a retrospective analysis of consecutive patients with liver disease related to NASH or HCV who received radiation segmentectomy with as initial treatment for HCC from 01/2017-07/2022.
- Eligibility criteria: solitary tumor ≤ 8 cm or up to 3 HCC ≤ 3 cm, ECOG 0-1, and absence of vascular invasion or extrahepatic disease.
- Imaging best response was assessed at 3- and 6-month follow-up. Target tumor and overall progression, TTP and OS were assessed. All outcomes were censored for liver transplantation.

RESULTS

- 142 patients included (NASH: 61; HCV: 81). Most had cirrhosis (NASH: 87%; HCV: 86%) and small tumors (median size NASH: 2.3 cm; HCV: 2.5 cm).
- NASH: higher BMI (p<0.001) & worse ALBI score (p=0.003).
- HCV: SVR in 73%. Higher frequency of Child-Pugh class A (NASH: 75%; HCV: 89%; p=0.037) and ALBI grade 1 liver function (NASH: 45%; HCV: 69%; p=0.008), younger age (p<0.001), and higher AFP levels (p=0.034).
- Similar median dose (NASH: 508 Gy; HCV: 452 Gy) and specific activity (NASH: 700 Bq; HCV: 698 Bq).

IMAGING RESPONSE PER MRECIST



COMPLETE PATHOLOGIC RESPONSE (CPN)

- | Group | CPN (%) |
|-------|---------|
| NASH: | 63% |
| HCV: | 54% |

SURVIVAL AND PROGRESSION OUTCOMES

- Mean non-censored follow-up: NASH 26.5 months (95%CI 22.6-30.3); HCV 33.2 months (95%CI 29.5-37.1). Mean censored follow-up: NASH 15.6 months (95% CI 12.4-18.8); HCV 20.5 months (95%CI 16.9-24.0).
- Non-censored OS: Not met for either cohort (p=0.25)
- Censored OS: NASH not met; HCV 53.9 months (95%CI 32.1-75.7) (p=0.15)
- Overall progression: 23 (38%) NASH- and 39 (48%) HCV-related HCC patients. Overall TTP: 17.4 months (95%CI 13.5-21.3) in NASH and 13.5 months (0.4-26.6) in HCV patients (p=0.86).
- Target tumor progression: 1 (2%) NASH- and 8 (10%) HCV-related HCC patients. Target tumor TTP: not met for either cohort (p=0.12).

DISCUSSION

- Total cohort: objective response rate of 98.6% and complete response of 87% per mRECIST.
- Radiation segmentectomy served as a neoadjuvant to liver transplantation in 42% of patients, with a combined CPN rate of 58%.
- Analysis by etiology of liver disease: comparable target tumor outcomes (ie, objective response, CPN, and target tumor progression, and TTP) with radiation segmentectomy in NASH- and HCV-related HCC.
- There were non-statistically significant trends in favor of the NASH cohort, with higher complete response rates, lower frequency of target tumor and overall progression, and longer overall TTP. It is not feasible to state if this is related to the target tumor, de novo HCC, or natural progression of underlying liver disease. This may suggest that patients with HCV-related HCC may best benefit from radiation segmentectomy with a shorter time to bridge to transplantation than those with NASH-related HCC.

CONCLUSIONS

- Although NASH and HCV are associated with different mechanisms of liver injury, patients with treatment naïve, early-stage HCC treated with radiation segmentectomy achieve comparable outcomes.

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